PATENT COOPERATION TREATY

PCT

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2005/001166	04.02.2005	06.02.2004

International Patent Classification (IPC) or both national classification and IPC
A61K9/107, A61K31/55, A61K31/164

Applicant
NOVARTIS AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Young, A

Telephone No. +49 89 2399-7811

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/001166

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 13

because:

☒ the said international application, or the said claims Nos. 13 with respect to Industrial Applicability relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-16
	No:	Claims	1
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-16
Industrial applicability (IA)	Yes:	Claims	1-12, 14-16
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III:

1. Claim 13 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V:

2. The documents considered in the present processing are consecutively numbered D1-D4; this numbering results from the citations D1-D4 found in the International Search Report (ISR) of the corresponding PCT application. It will be adhered to in the rest of the procedure. The cited passage(s) for each citation will be considered unless otherwise specified.

3. The application refers to a spontaneously dispersible pharmaceutical composition comprising a 5-aryl-4(R)-arylcarbonylamino-pent-2-enoic acid amide substance P antagonist. In a preferred embodiment a lipophilic component, a surfactant and optionally a hydrophilic component is further comprised.

4. Novelty, Art. 33(2) PCT
The subject-matter of claim 1 is considered to lack novelty over D1 and D2 under Article 33(2) PCT for the following reasons:
Claim 1 relates to a spontaneously dispersible pharmaceutical composition comprising a 5-aryl-4(R)-arylcarbonylamino-pent-2-enoic acid amide substance P antagonist. Besides the active agent there is no further technical feature disclosed to limit the pharmaceutical composition.
However, pharmaceutical compositions comprising the claimed active agent are already known from D1 or D2.

5. Inventive Step, Art. 33(3) PCT
The object underlying the present application is the provision of a spontaneously dispersible pharmaceutical composition comprising the claimed active agent to increase the bioavailability of the active agent.
The posed solution is a composition comprising a lipophilic component, a surfactant and optionally a hydrophilic component, preferably in the form of a microemulsion.

The claimed 5-aryl-4(R)-arylcarbonylamino-pent-2-enoic acid amide substance P antagonist are already known in the art (see D1 or D2). Also the most preferred compound according to claim 3 is already disclosed in the cited prior art (D1, claim 10 and D2, DNK-333).
These compounds are further known to be poorly water soluble, according to the description p.3.
It is common general knowledge in the art, that microemulsions enhance the bioavailability of poorly water-soluble drugs (D4) and that they can influence drug release from the formulation to enhance absorption or to lower toxicity (D3).
Thus, it seems purely conventional for the skilled artisan to prepare microemulsions of a known poorly water soluble drug in order to enhance the bioavailability.
This argumentation applies equally to the method claims.

For the foregoing reasons no inventive step can be acknowledged for the subject-matter of claims 1-16 within the meaning of Article 33(3) PCT.

6. For the assessment of the present claim 13 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

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see separate sheet

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Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-16
	No:	Claims	1
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-16
Industrial applicability (IA)	Yes:	Claims	1-12, 14-16
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III:

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5. Inventive Step, Art. 33(3) PCT
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